

## II. Request for Continued Examination

This response to the Office Action is filed with a request for continued examination ("RCE") after receipt by applicants of a final office action and with payment of the required fee. Hence the RCE is appropriate and the examiner is asked to withdraw the finality of the Office Action and enter this response.

### III. Claims Cancelled

Applicants hereby cancel claims 36, 40-41, 48-50, 53-54, 57-60 and 68-81, without prejudice to further prosecution at a later date.

The pending claims are therefore the twenty one claims 35, 37-39, 42-47, 51-52, 55-56 and 61-67.

#### IV. The Section 103(a) Rejection Over Wong

The Office Action rejected claims 35-81 under 35 U.S.C. section 103(a) as being unpatentable over Wong et al (U.S. patent 5,869,079. Respectfully, the rejection is in error and should be withdrawn.

As stated by the Office Action, the Wong reference discloses a PLGA implant containing dexamethasone. The Office Action states in numbered paragraph 7. on page 3 of the Office Action that since the instant claims are product claims an intended use does not provide a patentable distinction because "if a prior art structure (i.e. Wong) is capable of performing the intended use, then it meets the claim." (this statement is also repeated on page 6, numbered paragraph 12. of the Office Action). It is also noted by page 4, numbered paragraph 8. of the Office Action that while Wong does not teach the exact claimed formulations and rates of release, these claimed differences are obvious since Wong suggests changing the size and form of the implant and the Office Action cites to columns 7-8 of Wong for this point, noting that a person of ordinary skill would have been motivated to make such modification, to thereby arrive at the claimed invention.

In light of these comments in the Office Action applicants have amended the claims to limit the claims to an implant which clearly distinguishes over the implant disclosed by Wong. As explained below, the prior art structure of Wong is not capable of performing the intended use of the claimed subject matter, and therefore the amended claims are patentable over Wong.

The claims have been amended to add the following limitations to the claims:

1. "the implant being an extruded filament" (All Claims). This new claim limitation is supported by at least page 26, paragraph [0089] of Example 6 of the specification ("...filaments extruded...The resulting filaments...")

2. "the implant having a weight between about 500  $\mu\text{g}$  and about 1100  $\mu\text{g}$ " (All Claims). This new claim limitation is supported by at least page 18, paragraph [0062] of Example 1 of the specification ("...900-1100  $\mu\text{g}$ ..."), and by page 26, paragraph [0089] of Example 6 of the specification ("...500 $\mu\text{g}$  and 1000  $\mu\text{g}$ ...").

3. "the implant delivers at least about 20% of the agent within about 20 days in vitro". (Claims 35, 37-38, 42-47, 51 This new claim limitation is supported by at least: (1) Table 6 for replicate 1 on page 26 of the specification (note that by day 20 just over 30% of the agent had been released from the implant in vitro; (2) Table 6 for replicate 2 on page 27 of the specification (note that by day 20 almost exactly 20% of the agent had been released from the implant in vitro; (3) Table 7 for replicate 1 on page 28 of the specification (note that by day 20 over 23% of the agent had been released from the implant in vitro; (4) Table 7 for replicate 2 on page 28 of the specification (note that by day 20 just over 19% of the agent had been released from the implant in vitro.

3. "the implant delivers at least about 30% of the agent within about 20 days in vitro". (Claims 39, 52, 55-56 and 61-67). This new claim limitation is supported by at least Table 6 for replicate 1 on page 26 of the specification (note that by day 20 just over 30% of the agent had been released from the implant in vitro.; (2) Table 6 for replicate 2 on page 27 of the specification (note that by day 20 al

As noted by the last sentence of numbered paragraph 7., on page 4 of the Office Action: "Wong et al. also teach that the size and form of the implant can be used to control the rate of release, period of treatment , and drug concentration (column 7, lines 52-54)". Note that Wong then immediately states: "Larger implants will deliver a proportionately larger dose, but depending on the surface to mass ratio, may have a slower release rate."

All claims in the instant application have the limitation "without an added release modifier". Only (the first part of) Example 1 of Wong sets forth an implant which does not have a release modifier. The implants in Example 1 of Wong are extruded filaments weighing 100-120  $\mu\text{g}$ .

Example 1 at column 8, lines 44-46 of Wong states that the drug released very slowly from the small extruded filaments. Thus, as shown by FIG 1A of Wong after 20 days in vitro only about 10% of the drug had been released.

An implant shaped as a sheet, film, circular disc or plaque (see column 7, lines 39-40 of Wong) has a high surface area to mass ratio, as compared to an implant which is shaped as a filament (i.e. a rod shaped implant). As easily understood, an implant will release more drug if it has a high surface to mass ratio, as compared to an implant which has a lower surface to mass ratio (other factors [such as the absence of a release modifier] being held constant)

Thus, Wong found that small (100  $\mu\text{g}$  to 120  $\mu\text{g}$ ) filament shaped implants which do not have a release modifier release drug slowly (column 8, lines 44-48), and Wong states that although a larger implant can deliver more drug, it will have a slower release rate unless the surface to mass ratio is increased (i.e. change the shape of the implant from a filament to a sheet or film shape) (column 7, lines 53-56 of Wong).

Clearly, therefore Wong does not teach or suggest that a larger implant with the same shape ("filament") made in the same way ("extruded") and which therefore has the same surface to mass ratio, will release drug faster than a smaller extruded filament implant. In fact, Wong clearly teaches away from the claims as amended, which are limited to an extruded filament implant which releases at least 20% of the drug after 20 days in vitro. Wong states or at least strongly implies that to get such a faster drug release with a larger implant one must either use an implant which has a higher surface area to mass ratio, as

compared to a filament shaped implant, or (as done by Wong) use the same filament shaped implant but add one or more release modifiers (see Wong column 8, line 48, continuing to column 10.

For these reasons, the rejection over Wong should be withdrawn. See also *In re Soni*, 34 USPQ2d 1684-1692 (Fed. Cir. 1995) (reversing the Board decision affirming examiner's rejection of certain claims on the basis that once unexpected results are established, in the absence of contrary evidence, unexpected results successfully overcome the prima facie case of obviousness.

V. The Section 103(a) Rejection Over Wong and Guo


The Office Action rejected claims 48-50 and 68-70 under 35 U.S.C. section 103(a) as being obvious over the combination of Wong (U.S. patent 5,869,079) and Guo (U.S. patent 6,217,8951).

Claim 48-50 and 68-70 have been cancelled. Hence the rejection should be withdrawn.

VI. Conclusion

All issues raised by the Office Action have been addressed. Examination and allowance of claims 35, 37-39, 42-47, 51-52, 55-56 and 61-67 is requested.

Respectfully submitted,

  
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CERTIFICATE OF EXPRESS MAIL UNDER 37 C.F.R. § 1.10

I hereby certify that this Response to Office Action and the documents referred to as enclosed therein are being deposited with the United States Postal Service on this date **November 21, 2005** in an envelope as "Express Mail Post Office to Addressee" Mailing Label number EV 616125322 US addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Adriane Giberson

Name of person mailing paper

  
Signature of person signing paper

Date: November 21, 2005



**MARKED UP VERSION OF THE CLAIMS**

1-34. (Cancelled)

35. (Currently Amended) A bioerodible implant for treating an inflammation-mediated condition of an eye in an individual, the implant comprising a steroidal anti-inflammatory agent and a bioerodible copolymer without an added release modifier, the implant structured to be placed in the vitreous of the eye by being an extruded filament with a weight between about 500  $\mu$ g and about 1100  $\mu$ g which and releases delivers at least about 20% of the agent into the vitreous within about 20 days in vitro~~after the implant has been placed in the vitreous of the eye in an amount sufficient to reach an in vivo concentration equivalent to at least about 0.05  $\mu$ g/ml dexamethasone within about 48 hours and to maintain an in vivo concentration equivalent to at least about 0.03  $\mu$ g/ml dexamethasone for at least about three weeks.~~

36. (Cancelled).

37. (Previously presented) The implant according to claim 35, wherein the steroidal anti-inflammatory agent is selected from the group consisting of cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone and mixtures thereof.

38. (Previously presented) The implant according to claim 35, wherein the steroidal anti-inflammatory agent is dexamethasone.

39. (Currently Amended) The implant according to claim 35, ~~which wherein the implant releases at least about 30% of is structured to deliver the agent after about 20 days in vivo to the vitreous in an amount sufficient to reach an in vivo concentration equivalent to at least about 0.1 µg/ml dexamethasone within about 48 hours and to maintain an in vivo concentration equivalent to at least about 0.03 µg/ml dexamethasone for at least about three weeks.~~

40-41. (Cancelled).

42. (Previously presented) The implant according to claim 35, wherein the steroidal anti-inflammatory agent comprises about 50 to about 80 weight percent of the implant.

43. (Previously presented) The implant according to claim 42, wherein the steroidal anti-inflammatory agent comprises about 70% by weight of the implant.

44. (Previously presented) The implant according to claim 35, wherein the bioerodible copolymer is a polyester.

45. (Previously presented) The implant according to claim 44, wherein the bioerodible copolymer is polylactic acid polyglycolic acid (PLGA) copolymer.

46. (Previously presented) The implant according to claim 35, wherein the inflammation mediated condition of the eye to be treated is selected from the group consisting of uveitis, macular edema, macular degeneration, retinal detachment, ocular tumors, fungal infections, viral

infections, multifocal choroiditis, diabetic uveitis, proliferative vitreoretinopathy (PVR), sympathetic ophthalmia, Vogt Koyanagi-Harada (VKH) syndrome, histoplasmosis, and uveal diffusion.

47. (Previously presented) The method according to claim 46, wherein the inflammation mediated condition of the eye to be treated is uveitis.

48-50 (Cancelled).

51. (Previously presented) The implant according to claim 35, wherein the individual whose eye is to be treated is a human.

52. (Currently Amended) An implant for treating an inflammation-mediated condition of the eye in an individual, comprising a solid body structured for placement into the vitreous of the eye by being an extruded filament with a weight between about 500  $\mu$ g and about 1100  $\mu$ g which releases at least about 30% of the agent within about 20 days in vitro~~after, said body comprising particles of a steroidal anti-inflammatory agent entrapped within a bioerodible polymer without an added release modifier, whereby said agent is released from the body by erosion of the polymer, and whereby said agent is delivered to the vitreous at a rate and for a time sufficient to reach an in vivo concentration equivalent to at least about 0.05  $\mu$ g/ml dexamethasone within about 48 hours, and to maintain an in vivo concentration equivalent to at least about 0.03  $\mu$ g/ml dexamethasone for at least about three weeks.~~

53-54. (Cancelled)

55. (Currently Amended) The implant according to claim 52~~3~~, wherein the steroidal anti-inflammatory agent is selected from the group consisting of cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone and mixtures thereof.

56. (Currently Amended) The implant according to claim 53~~2~~, wherein the steroidal anti-inflammatory agent is dexamethasone.

57-60. (Cancelled)

61. (Currently Amended) The implant according to claim 52~~3~~, wherein the steroidal anti-inflammatory agent comprises about 50 to about 80 weight percent of the implant.

62. (Previously presented) The implant according to claim 61, wherein the steroidal anti-inflammatory agent comprises about 70% by weight of the implant.

63. (Previously presented) The implant according to claim 61, wherein the steroidal anti-inflammatory agent comprises about 50% by weight of the implant.

64. (Currently Amended) The implant according to claim 52~~3~~, wherein the bioerodible copolymer is a polyester.

65. (Currently Amended) The implant of claim 523, wherein the bioerodible copolymer is polylactic acid polyglycolic acid (PLGA) copolymer.

66. (Currently Amended) The implant according to claim 523, wherein the inflammatory mediated condition of the eye to be treated is selected from the group consisting of uveitis, macular edema, macular degeneration, retinal detachment, ocular tumors, fungal infections, viral infections, multifocal choroiditis, diabetic uveitis, proliferative vitreoretinopathy (PVR), sympathetic ophthalmia, Vogt Koyanagi-Harada (VKH) syndrome, histoplasmosis, and uveal diffusion.

67. (Previously presented) The implant according to claim 66, wherein the inflammation-mediated condition of the eye to be treated is uveitis.

68-81 (Cancelled).